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Assessment of Bone Density in Children 6 to 14 Years Old with Asthma Treated with Fluticasone

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ABSTRACT

BACKGROUND AND OBJECTIVE: Corticosteroid therapy is one of the main treatments for asthma and considering the effects of corticosteroid on bone mineral density, the present study was conducted to analyze the bone mineral density in children with asthma treated with inhaled corticosteroids.

METHODS: This cross-sectional study was conducted among 62 children 6 to 14 years old with moderate or severe asthma admitted to Amirkola Children's Hospital, whose disease have lasted for at least one year and were treated with inhaled corticosteroids. DEXA method was used to measure bone density using Hologic QDR4500 device. Based on this method, the lumbar spine and the femur neck was examined and Z-Score criteria was recorded for each patients. In addition to the above-mentioned information, the dosage, duration of consumption and duration of the disease was also recorded for each patients.

FINDINGS: The mean age of children was 7.8 ± 2.1, among which 33 children (53.2%) were boys. The mean duration of asthma was 2.3 years and the mean forced expiratory volume in 1 second (FEV1) was 77.3±5.4% in patients. Osteopenia was observed in 5 patients (CI-95%=1–15, 8.1%). There was no significant difference between osteopenia and gender, duration of consumption and age. However, there was a significant difference between osteopenia and the dosage of the drug (p=0.007).

CONCLUSION: Osteopenia was observed in a considerable percentage of children with asthma who were treated with fluticasone spray for more than one year, which was also affected by drug dosage.

KEY WORDS: *Asthma, Fluticasone, Bone Density*.

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Allergic diseases, especially asthma, are among the chronic and prevalent diseases of childhood in developing countries, including Iran (1, 2). Multiple reports indicate an increase in the incidence and severity of the complications of this disease throughout the world (3-5). Common remedies for this disease are corticosteroids. Oral corticosteroids can reduce bone mineral density and cause osteoporosis in adults (6). Studies have shown that both the daily dose and the cumulative dose are associated with osteoporosis and increase risk of bone fractures (7, 8). Short courses (more than 2.5 episodes per year) have been associated with decreased bone mineral density in adults with asthma (9). However, cross-sectional studies on the effect of oral corticosteroids on bone mineral density or risk of fracture was accompanied with controversial results (10-13). Studies in children and adults about the effect of inhaled corticosteroids on bone mineral density and fracture risk have also been associated with controversial outcomes (11, 14-25). Therefore, the aim of this study was to determine the severity of bone mineral density in children with asthma referring to Amirkola Children's Hospital.

Methods

This cross-sectional study was performed on 62 children aged 6 to 14 years old with moderate or severe asthma with a minimum duration of one-year treatment with inhaler Fluoticasonepropionate, which was referred to Amirkola Children's Hospital. Regular use of vitamin D, vitamin D deficiency, physical and motor disabilities, anticonvulsants drugs, diabetes, thyroid dysfunction and inability to perform spirometric peak were excluded. The number of samples was obtained from the study of Paoli de Valeri et al. (26) and using the appropriate formula for 62 children with asthma. Sampling was non-probabilistic and purpose-based. The criterion for asthma diagnosis was based on GINA criteria according to history-clinical examination and, if necessary, respiratory function tests (27).

IgE and serum eosinophil count were measured. In allergic patients, such as asthma, IgE generally rises. In all patients, total IgE was measured to determine high IgE levels. All patients were then evaluated for bone density. Bone densitometry was performed using the Dual-Energy X-ray absorptiometry (DEXA) method using the Hologic QDR4500 (US) device, in which the lumbar spine and femoral neck were evaluated and the Z-score for each person was registered. Z-Score is a method for determining osteoporosis associated with osteopenia and osteoporosis.

A reduction of 1 to 2.5 standard deviations from the normal number for age and sex as osteopenia and a reduction of more than 2.5 deviations is considered as osteoporosis (28, 29). In addition to the above information, the dose, duration of use and duration of the disease were also recorded for each individual. Respiratory and dentometric tests were performed by an individual by an asthma specialist and allergy specialist and a nuclear medicine specialist, respectively.

Since danitometry is not routinely performed in patients with asthma who receive inhaler corticosteroids, therefore, patients with informed consent of parents entered the study. Regarding the dose of Fluoticasone, a low dose were 100 to 200 micrograms per day and a moderate dose were 200 to 400 micrograms for the age of 6 to 11 years and 300 to 500 micrograms for over 12 years of age and high doses above 400 for those aged 6 to 11 years and above 500 micrograms for over 12 years. Data were analyzed using SPSS15 software, Chi-square and Fisher's exact tests, and $p < 0.05$ was considered significant.

Result

The mean age of children with asthma was 7.8±2.1, ranging from 6 to 14 years old. 33 (53.2%) of the children were boys and 29 (46.8%) were girls. Duration of asthma and FEV1 were 2.3±0.9 and 77.3±5.4, respectively. Eosinophilic and IgE levels increased by 40.3% and 48.4% of patients (table1).

Table 1. Distribution of eosinophilic status, IgE, symptoms and fluticizone consumption in asthmatic patients

Group		N(%)
Eosinophil count	normal	37(59.7)
	increased	25(40.3)
IgE value	normal	32(51.6)
	increased	30(48.4)
Asthma symptoms	Wheeze+dyspnea+ cough	61(98.4)
	Shortness of breath + cough	1(1.6)
Duration of consumption	One year	31(50)
	two years	31(50)
Dosage	Low dose	27(43.5)
	Medium dose	25(40.3)
	High dose	10(16.1)

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Osteopenia was present in 5 (8.1%) patients with a 95% confidence interval of 1 to 15%, and 57 (91.9%) patients had normal bone density. The percentage of osteopenia in girls was slightly higher than of boys but did not have a significant difference (table 2). Also, the percentage of osteopenia in children taking fluoticasone for 2 years was more than those who took the drug for one year, but this difference was not statistically significant. However, the difference in osteopenia was significant in terms of dosage, while the percentage of osteopenia in low-dose, zero-dose and high-dose users was 30%. The mean age of patients with osteopenia (2.7±6.7) and normal group (2.2±7.8) was not significantly different.

Table 2. Distribution of osteopenia according to sex and fluticizone consumption in asthmatic children.

Variable		Normal N(%)	Osteopenia N(%)	P-value
Sex	Boy	31(93.9)	2(6.1)	0.658
	Girl	26(89.7)	3(10.3)	
Duration of consumption	One year	29(93.5)	2(6.5)	1
	two years	28(90.3)	3(9.7)	
Dosage	Low dose	27(100)	-	0.007
	Medium dose	23(92)	2(8)	
	High dose	7(70)	3(30)	

Discussion

The results of this study showed that osteopenia was observed in a significant percentage of children with asthma that had been treated with fluoticasone spray for more than one year. In a study by Behmanesh et al in children with asthma receiving long-term inhaled corticosteroids, 30 children aged 5-15 years with asthma who received more than 400 µg fluticasone propionate spray in a day for more than 6 months, bone density was measured by DXA (Dual Energy Xray absorptiometry) method.

The results showed that in comparison with bone density, standardized healthy children and according to age, sex, race, height, weight and bone area, 18 patients (60%) had decreased bone density and Z. Score was between 1 and 2.5 (30) or in a study by Mori et al, the risk of osteoporosis in children taking oral corticosteroids and inhalants was 35%, in children taking oral corticosteroid was 28% and in control group was 10% (31). Also, in a study by Allen et al, 48 children with pre-pubertal asthma were studied with 9 healthy children that use of inhaled corticosteroid for 9 to 20 months significantly reduced the mineral density of asthmatic children compared to the control group (32). The values obtained in our study were lower than other studies, which may be due to the dose of the drug, because in the Behmanesh et al study, only children who were taking the medicine at high doses were included. However, it is noteworthy that the side effects of corticosteroids in inhaled intake are less than oral intake, in a study conducted by Mori et al, the risk of osteoporosis in children taking oral corticosteroid and inhalation were 35%, in children who only had inhaled corticosteroid use were 28% and in the control group were 10% (31) or in a systematic review and meta-analysis by Hansen et al, on the effect of systemic glucocorticoid on bone density and fractures in children finally, 16 studies were reviewed and the results showed that bone density in the lumbar spine was significantly lower in the children treated with the same age than the control group.

Bone density was significantly lower in children who consumed glucocorticoids than children who had the same disease but did not take glucocorticoids (33). Also, a study by Fuhlbrigge et al, reported that long-term use of inhaled corticosteroids on bone density is less than oral corticosteroids, and the use of proper nutritional regimens containing sufficient amounts of vitamin D and calcium can prevent or limit the effects of corticosteroids on bone (34).

The results of this study showed that the distribution of osteopenia did not have a significant relationship with gender, age, duration of use, which was probably due to the low number of samples for the study of this relationship, but the relationship between osteopenia and dose was statistically significant, so that low-dose of fluoticasone did not show osteopenia doses and in high doses, the percentage of osteopenia was high. A study by Wheelock et al, reported that moderate to low doses of inhaled corticosteroids (less than 1500 µg beclomethasone) did not significantly decrease bone density after 2 to 3 years of follow up, but higher doses increased the risk of non-traumatic fractures were observed in follow up of 1-4 years (25), which is similar to the results of this study, or in a study by Galván Fernández et al, on 151 children aged 1 to 17 years, 71 asthmatic children who had at least with 6 months inhalation Corticosteroid therapy was followed by (group I) with 44 asymptomatic children who were consumed while an attack (group 2) and 36 healthy children (Group 3) in terms of bone mineral density, there were significant differences of bone density

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between groups 1 and 2, but there was no significant difference between groups 1 and 3 (27). Therefore, considering the significant percentage of asthmatic children treated with inhaled corticosteroids with osteopenia, bone density measurement is recommended in all children with asthma receiving long-term inhaler corticosteroids, and in particular with high dose recipients. Also the minimum dose can be used to control asthma, or teach the parents how to properly use the drug to reduce systemic absorption. The limitation of the present study was the lack of control group. The results of this study showed that osteopenia was observed in a significant proportion of children with asthma who had been treated with flotticasone spray for more than a year. There was also a relationship between the dose of flotticasone and osteopenia.

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